National Cancer Medicines Advisory Group (NCMAG) Programme

NCMAG101 Abiraterone | Advice Document

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Abiraterone acetate plus prednisolone in combination with androgen deprivation therapy for the treatment of high-risk hormone-sensitive non-metastatic prostate cancer

NCMAG Decision| Routine off-label use is **not supported for the originator abiraterone product. The proposal will undergo a health economic re-evaluation and prioritised review by NCMAG once generic abiraterone products are available.**

Decision Rationale

Phase III study data shows the abiraterone combination improves metastases-free survival compared with androgen deprivation therapy alone. However, the health benefits in relation to the treatment costs were not sufficient to gain support from the NCMAG Council. Once generic alternatives are available, NCMAG will re-evaluate the health economics and review the proposal.

Proposal Details	
Medicine name	Abiraterone
Cancer type	Prostate Cancer
Proposed off-label use	High-risk hormone-sensitive non-metastatic cancer: 2 years of abiraterone with radical radiotherapy to the prostate and 3 years of androgen deprivation therapy (ADT)
Medicine Details	Form: Film-coated tablets Dose: 1,000mg once daily
Treatment Marketing Authorisation	• The treatment of newly diagnosed high-risk metastatic hormone-sensitive prostate cancer (mHSPC) in adult men in combination with ADT[1]. • The treatment of metastatic castration resistant prostate cancer (mCRPC) in adult men who are asymptomatic or mildly symptomatic after failure of ADT in whom chemotherapy is not yet clinically indicated[1]. • The treatment of mCRPC in adult men whose disease has progressed on or after a docetaxel-based chemotherapy regimen[1].

1.0 Current Management Context

Symptoms of non-metastatic prostate cancer include urinary symptoms, erectile problems, blood in the urine or unexplained back pain[2]. Stage 3 prostate cancer has a five year Overall Survival (OS) of 95% and stage 4 prostate cancer has a five year OS rate of 49%[3]. Both Stage 3 and Stage 4 patients are potentially eligible for treatment with abiraterone within this off-label use. Abiraterone inhibits CYP17 intracellular production of testosterone within the adrenals and prostate cancer cells. It is necessary to administer a glucocorticoid (usually prednisolone) to reduce mineralocorticoid excess[1]. Testosterone plays a central role in driving prostate cancer growth. Orchiectomy or ADT reduce endogenous testosterone production, however prostate cancer may become resistant and progress despite a low testosterone environment. Second generation androgen inhibitors (abiraterone, enzalutamide, apalutamide and darolutamide) offer a more complete blockade of testosterone production and/or action[4].

Differences in the definition of high-risk and localised disease exist between international guidelines. This management summary is in the context of systemic therapy for locally advanced or high risk non-metastatic prostate cancer and applies to patients who undergo definitive local treatment with radical radiotherapy[5].

The National Institute for Health and Care Excellence (NICE)[6] and the European Society for Medical Oncology (ESMO)[7] guidelines recommend external beam radiation therapy (EBRT) and long-term ADT (>2 years) for high-risk non-metastatic or locally advanced disease with the addition of neoadjuvant docetaxel for six cycles on a case-by-case basis for young, fit patients. For node positive disease the National Comprehensive Cancer Network (NCCN) recommends abiraterone as an option in combination with ADT and EBRT. For node negative disease NCCN recommends either docetaxel or abiraterone as an option for very high-risk disease only. NCCN disease characteristics for very high-risk disease are at least one of the following; clinical stage cT3b-cT4, Primary Gleason pattern 5, 2 or 3 high-risk features, >4 cores with grade 4 or 5 disease)[8].

A recent guideline from the European Association of Urology (EAU)[9] includes the addition of 2 years of abiraterone to EBRT and ADT as an option for patients who match the STAMPEDE population. Within NHSScotland the standard of care (SOC) for patients undergoing radical treatment is EBRT and ADT in the high-risk non-metastatic disease (M0) setting and therefore the most relevant comparator for this proposal is usually EBRT and long-term (2-3 years) ADT. Six cycles of docetaxel may be added for selected patients with high-risk disease. The addition of docetaxel may be an option in patients who are young and have minimal co-morbidity as it increases time to relapse.

2.0 Evidence Review Approach

A literature search to identify clinical and economic evidence was conducted on key electronic databases including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, major international health technology agencies, as well as a focused internet search. The search strategy comprised both Medical Subject Headings and keywords. The main search concepts were abiraterone, non-metastatic, high-risk and prostate cancer. No filters were applied to limit the retrieval by study type. Two health services researchers independently screened titles and abstracts: eligible full text articles were retrieved and assessed for inclusion. The included publications were critically appraised using the following tools: The Cochrane risk of bias 2.0 tool and the ISPOR (International Society for Pharmacoeconomics and Outcomes Research) Questionnaire to Assess the Relevance and Credibility of Network Meta-Analysis.

2.1 Evidence Review Summary | Clinical efficacy evidence

The key evidence to support the use of abiraterone in the proposed population includes data from the Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy multi-arm, multi-stage (MAMS) STAMPEDE platform[10]; included studies can be found in Table 1.

Table 1 Summary of studies relevant for this proposed use in non-metastatic prostate cancer

Author	Study design	Comparison
Attard et al 2022	Pooled analysis of data from two trials within the MAMS platform	ADT versus ADT, abiraterone and prednisolone with or without enzalutamide
James et al 2017	Phase III RCT	ADT versus ADT, abiraterone and prednisolone
Rajwa et al 2022	Network Meta-analysis	A combination of systemic treatments including ADT plus chemotherapy or an androgen receptor signaling inhibitor with ADT

Key: MAMS = multi arm multi stage; ADT = androgen deprivation therapy; RCT = randomised controlled trial

Comparison of ADT versus the abiraterone combination with or without enzalutamide

Attard and colleagues combined data from two open-label randomised controlled phase III trials conducted to assess the efficacy of adding abiraterone and prednisolone with enzalutamide (enzalutamide trial) or without enzalutamide (abiraterone trial) to ADT in men with high-risk M0 prostate cancer who are treated with ADT for three years, combined with radiotherapy. Eligible

patients had no evidence of distant metastases on imaging and a World Health Organisation (WHO) performance status (PS) 0-2. Patients were either N1 (with nodal involvement) or, if N0 (no nodal involvement), either high-risk (tumour stage T3 or T4, Gleason sum score of 8–10, or prostate-specific antigen (PSA) concentration ≥40ng/mL) or relapsing with high-risk features (≤12 months of ADT with an interval of ≥12 months without treatment and a PSA concentration ≥4 g/mL with a doubling time of <6 months or a PSA concentration ≥20ng/mL). Patients with confirmed clinically significant cardiovascular disease (such as severe angina, myocardial infarction less than 6 months prior to randomisation, or a history of cardiac failure) were excluded[10].

Patients in the abiraterone trial were randomly assigned (1:1) to either receive ADT alone (n=455), which could include surgery and luteinising-hormone-releasing hormone agonists or antagonists, or in combination with oral abiraterone acetate (1,000mg daily) and oral prednisolone (5mg daily) (abiraterone combination group; n=459). In the enzalutamide trial patients were also randomly assigned (1:1) to either ADT alone (n=533) or abiraterone combination with enzalutamide (160 mg daily orally) (n=527). In both trials randomisation was stratified by nodal status, age, performance status, plan for radiotherapy, type of ADT, use of regular non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin at baseline and recruiting centre[10].

A preplanned subgroup analysis was conducted for metastasis-free survival (MFS) and overall survival to evaluate the consistency of effect between the two studies. The baseline characteristics were well balanced between trials, mean age was 68 years (IQR 63-74), median PSA was 34ng/ml (IQR 15-74), 39% of patients were node positive and 79% had a Gleason score sum of 8-10. Medium follow-up was 85 months (IQR 83-86) and 60 months (IQR 59-71) in the abiraterone and the enzalutamide trials respectively[10].

The primary study outcome was MFS, defined as the time from randomisation to death from any cause or to distant metastases confirmed by imaging, assessed by unblinded investigators, in the intention-to-treat population. One hundred and eighty MFS events were reported in the abiraterone combination with or without enzalutamide groups and 306 in the ADT groups. Metastasis-free events were reported as follows for the abiraterone combination with or without enzalutamide groups versus the ADT groups at 24 months, 48 months and 72 months, respectively - 41 versus 83, 102 versus 195, and 157 versus 272. Metastasis-free survival was significantly longer in the abiraterone combination with or without enzalutamide groups (hazard ratio [HR] 0·53, 95% CI 0·44-0·64, p<0.001), median MFS was not reached in either group. Sub-group analysis for MFS detected a trend suggesting a difference for the following factors: 'WHO PS (0/1-2)' and 'use of NSAIDs or aspirin; (No/Yes)'[10]. The effect sizes for the group with a WHO PS of 0 and with a WHO PS of 1-2 are HR 0.47 (95%CI 0.38-0.58) and HR 0.86 (95%CI 0.58-1.28), respectively[10]. The effect sizes for regular NSAID/aspirin use - No and Yes are HR 0.62 (95%CI 0.51-0.77) and HR 0.32

(95%CI 0.21-0.48), respectively[10]. The secondary outcomes of overall survival, prostate cancer specific survival, PFS and biochemical failure-free-survival also favoured the abiraterone combination with or without enzalutamide groups over the ADT groups; HR 0·60 (95% CI 0·48-0·73), HR 0·49 (95% CI 0·37-0·65), HR 0·44 (95% CI 0·36-0·54) and HR 0·39 (95% CI 0·33-0·47), respectively. A pre-specified analysis of the individual abiraterone and enzalutamide trials showed a consistent overall effect for abiraterone with and without enzalutamide for MFS, (abiraterone trial, HR 0·54 [95% CI 0·43-0·68]; enzalutamide trial, 0·53 [95% CI 0·39-0·71]), indicating no benefit from the addition of enzalutamide to abiraterone.

Comparing ADT with the abiraterone combination

A further study by James et al 2017 using the STAMPEDE data compared the use of the abiraterone combination (n=960) with ADT (n=957) in patients with newly diagnosed and metastatic, node-positive, or high-risk locally advanced prostate cancer[11]. One hundred and eighty-four deaths were reported in the abiraterone combination group and 262 in the ADT group. Overall survival was significantly longer in the abiraterone combination group than the ADT group (hazard ratio [HR] 0·63, 95% CI 0·52-0·76), median MFS was not reached in either group. There was no evidence of treatment effect by metastatic status (M0, HR 0.75 [95% CI 0.48–1.18)]; M1, HR 0.61[95% CI 0.49–0.75]). The information from this study and the favouring of the abiraterone combination over ADT were used to inform the economic evaluation presented below. Comparing the results from this study by James et al 2017 with the study by Attard et al 2022 provides reassurance that the data used in the economic model is directionally consistent with more recent data.

Network Meta-Analysis of treatments in non-metastatic unfavourable prostate cancer

The systematic review and NMA was conducted to investigate the effect of adding combination systemic treatment to primary definitive local therapy in patients with high-risk and/or unfavourable non-metastatic prostate cancer[12]. Studies were included if the population had undergone neoadjuvant/adjuvant combined systemic therapy (which had to include ADT plus chemotherapy or an androgen receptor signalling inhibitor) and was being compared to patients receiving ADT only, other antiandrogens agents, or observation. Efficacy data for the abiraterone combination came from the Attard study described earlier. The NMA for patients treated with radiotherapy for non-metastatic prostate cancer included 6 studies, with the Attard study providing the only data for the abiraterone combination. It was conducted for direct and indirect treatment comparisons with the comparisons and results relevant to this proposed use shown in Table 2. For MFS, the Surface Under the Cumulative Ranking (SUCRA) results indicated that the preferred treatment probability was 82% for the abiraterone combination, 32% for docetaxel plus ADT, and 1.5% for ADT[12].

Table 2: Network Meta-analysis Results[12]

Comparison	Outcome			
	Overall survival	Cancer-specific survival	Metastasis-free survival	Failure-free survival
	HR(95%CI)	HR(95%CI)	HR(95%CI)	HR(95%CI)
Abiraterone plus ADT versus ADT	0.63 (0.48-0.82)	0.52 (0.36-0.75)	0.54 (0.41-0.72)	0.39 (0.31-0.49)
Abiraterone plus ADT versus docetaxel plus ADT	0.69 (0.50-0.95)	0.76 (0.44-1.33)	0.63 (0.45-0.88)	0.53 (0.41 - 0.70)
Key: HR = hazard ratio; CI = confidence interval; ADT = androgen deprivation therapy NMA used random-effects models				

2.2 Evidence Review Summary | Safety evidence

Attard et al reported that 37% (169/451) of patients in the abiraterone combination group versus 29% (130/455) of patients in the ADT group had grade 3 or worse adverse events (AE) during the first 24 months[10]. Three grade 5 AEs were reported in the abiraterone combination group versus zero in the ADT group (one event each of rectal adenocarcinoma, pulmonary haemorrhage, and a respiratory disorder). The most common adverse event grade 3 or worse for the abiraterone combination group versus the ADT group were: erectile function (9% versus 11%), hypertension (5% versus 1%) and alanine transaminase (5% versus 0%)[10]. The median time to stopping abiraterone was 23.7 months (IQR: 17.6-24.1 months) in the abiraterone combination group.

This safety profile for the abiraterone combination in non-metastatic patients is consistent with the known abiraterone safety profile and similar to the safety profile seen in studies for on-label uses.

The SUCRA score for the NMA show the preferred treatment probability with regard to grade ≥3 AEs was 92% for ADT, 66% for the abiraterone combination, and 20% for docetaxel plus ADT[12].

2.3 Evidence Review Summary | Clinical effectiveness considerations

Quality assessment of key clinical evidence

Overall, the included trials were assessed to have a low risk of bias (RoB) concerns using the Cochrane RoB-2 tool[10]. All the STAMPEDE studies were open-label and may be at risk of performance bias, affecting patient-reported outcomes, and assessment bias. Patients in the ADT groups may have received second generation hormone treatments on progression of their cancer.

The application of the ISPOR questionnaire for the NMA identified the following issues: the NMA was relevant to the proposal in terms of population, interventions and outcomes[12]. The

methodology was considered robust, although, some areas of the analysis were weak, such as the lack of justification for random effects model and no assessment of consistency between the indirect and direct evidence[12].

There is variation in the definition of high-risk non-metastatic disease

Approximately 15-30% of prostate cancer patients will present with high-risk localised or locally advanced prostate cancer[13, 14]. There are variations in definition of high-risk cancer with most international consensus guidelines stipulating the criterion for PSA being >20ng/ml for high-risk, node negative cancer. The STAMPEDE platform used a stricter PSA cut-off of >40ng/ml, therefore potentially included patients with a higher risk of micrometastatic prostate cancer who would benefit more from additional systemic therapy[5].

Not all patients in the study received radiotherapy and the relative treatment effect of abiraterone appears consistent across the groups that did and did not receive radiotherapy.

For node positive disease SOC in NHS Scotland is to combine EBRT with ADT in patients undergoing definitive local treatment[6, 7, 9]. The STAMPEDE platform did not mandate radiotherapy for node positive disease with 29% of patients not receiving radiotherapy[5]. However, the relative treatment effect for abiraterone in combination with ADT compared to ADT alone appeared to be consistent between patients who did receive radiotherapy and those who did not receive radiotherapy.

Overall, results based on the population and concomitant treatments in STAMPEDE are likely to be generalisable to use in NHSScotland

The STAMPEDE platform protocol enrolled patients who were due to start ADT and must not have had greater than 12 weeks ADT prior to enrolment, with patients having a minimum of 2 years of ADT if receiving radiotherapy and indefinite if not receiving radiotherapy[5]. Randomisation was stratified for type of ADT. There is variation in duration of ADT across NHSScotland, ranging from 2 to 3 years. The STAMPEDE meta-analysis and STAMPEDE trial do not report durations of ADT between the control and intervention arms[10]. However, if these did differ it could pose a confounding factor.

The STAMPEDE platform recommended seventy-four Gy in thirty-seven fractions to the prostate and seminal vesicles or the equivalent using hypofractionated schedules[5]. These regimens are considered SOC in Scotland. Radiotherapy treatment within the STAMPEDE platform can be considered generalisable to current practice within Scotland[5].

Metastasis-free survival is an appropriate surrogate outcome for overall survival in prostate cancer

Metastasis-free survival is a strong surrogate for OS for localised prostate cancer that is associated with a significant risk of death from prostate cancer and is an appropriate outcome measure[15]. The

observed benefit of OS in the combination-therapy groups compared to the control groups is also supportive of the use of MFS as a surrogate measure[10].

Interpreting overall survival results

At the time of analysis of the abiraterone study, 19% (383/1974) of patients had died and the median overall survival had not been reached in either the abiraterone or control group. The improved OS (6-year survival rates for combination therapy versus control were 86% and 77%), in addition to extended MFS for the abiraterone regimen is reassuring. There is a lack of information about subsequent treatments after stopping randomised study treatment and patients in the control arm would have been able to receive second-generation hormone treatments on progression within trials or as SOC since 2019[10]. Within the STAMPEDE platform almost all (99.2%) patients were recruited from the UK therefore the subsequent treatments may reflect practice and support the generalisability of the OS result[16].

The STAMPEDE platform has wide eligibility criteria and recruited predominantly from a UK population. However, only 18% of patients had a WHO performance status of 1-2, therefore this may impact on the generalisability to the Scottish population. The sub-group analysis in the STAMPEDE meta-analysis detected a difference in efficacy between WHO PS 0 compared to WHO PS 1-2[10]

Based on indirect evidence the abiraterone regimen extends metastasis-free survival compared with the docetaxel regimen

Docetaxel in addition to SoC may be an option for a small proportion of patients; those who are younger and fit[6-9].

The NMA reported statistically significant improvements in OS and MFS for the abiraterone combination over the docetaxel combination. The NMA supports the use of abiraterone in patients who would normally receive combination ADT and EBRT as well as patients who would otherwise receive neo-adjuvant docetaxel in combination with ADT and radiotherapy[12].

2.4 Evidence Review Summary | Benefit-risk balance

Abiraterone in combination with ADT and EBRT improves 6-year metastasis-free survival from 69% to 82% and OS at 6 years from 77% to 86%. Abiraterone is well tolerated with no identified unexpected side effects in this off-label population compared to its licensed indications. There was an increased rate of high blood pressure with combination treatment, however there was no signal for increased cardiac events in comparison to ADT alone. The NMA also demonstrated a favourable side effect profile for abiraterone plus ADT in comparison to docetaxel plus ADT.

2.5 Council Review | Benefit-risk balance evaluation

After consideration of all the available evidence regarding the clinical benefits and risks, the Council were satisfied that the case had been made for the clinical effectiveness of abiraterone in high-risk non metastatic hormone sensitive prostate cancer.

3.0 Evidence Review Summary | Economic evidence

One economic study was identified through contact with the STAMPEDE study team[17]. The lead author provided additional points of clarification on the methods used in the economic study.

Type of economic evaluation

The study was a trial based economic evaluation, using cost and outcome data from the STAMPEDE platform (data cut off February 2017), to generate results using an individual patient level simulation with a lifetime time horizon[11]. The study perspective was indicated to be from an English NHS perspective. The type of economic evaluation was a cost-utility analysis.

Population, intervention, comparator and outcomes

The population used in the study was patients with high-risk, locally advanced metastatic or recurrent prostate cancer starting first-line hormone therapy. Subgroups based on non-metastatic and metastatic disease were provided in the results section. The intervention was AAP (abiraterone acetate 1000mg/day plus prednisolone 5mg/day) plus SOC (standard of care). SOC was hormone therapy for at least 2 years with radiotherapy in pre-selected patients. The comparator was SOC alone. Outcomes of the economic model were survival (years) and quality adjusted life years (QALYs).

Costs

Costs included were intervention and comparator medicine, monitoring, subsequent medicines (docetaxel, enzalutamide, cabazitaxel and radium-223), general disease management, serious adverse events, and end of life care. A 3.5% annual discount rate for both costs and QALYs was applied.

Key results and method of uncertainty assessment

For the non-metastatic subgroup, the base-case ICER was £149,748 per QALY gained for AAP plus SOC. The incremental mean per-patient cost for the non-metastatic group was £48,821. This was primarily driven by the acquisition cost of abiraterone. The incremental mean per-patient QALYs were 0.33 in the non-metastatic group. This was primarily driven by the increased time spent in the hormone naive health states. The base case ICER of £149,748 does not take into account the

confidential patient access scheme (PAS) discounts available for medicines. Deterministic sensitivity analysis was performed on the cost of abiraterone. For the ICER to be below a £30,000 threshold, the cost of abiraterone would need to decrease to 29% of its current BNF price in the non-metastatic patient group. If the cost of abiraterone was 11.7% of the current BNF price, AAP plus SOC would be cost-saving in this patient group compared to SOC alone. Uncertainty of results was primarily assessed using probability sensitivity analysis.

3.1 Evidence Review Summary | Cost-effectiveness considerations

Consistency with the STAMPEDE platform[5]

As the economic study was developed from a trial-based analysis, this allowed for consistency with the James et al 2017 study. The population, intervention and comparator were therefore equivalent. Access to individual patient level data facilitated the creation of an individual patient level simulation, with a model structure that used appropriate health states to capture disease progression from hormone naive to castration resistant. Survival functions were derived using outcome data from James et al 2017 and used to simulate patient transition between health states[11]. Certain survival functions and transitions within the model were reflective of the primary and intermediate primary outcomes, such as a joint survival function to model failure free survival. The study noted validation exercises of the survival functions, comparing to other published work, with agreeable results. A comprehensive set of costs were included in the model, with unit costs taken from standard UK sources, and regression methods used to overcome challenges in using the cost data. Utility values were obtained from James et al 2017, with the imputation methods used to overcome issues of missing data showing robustness[11].

Comprehensive reporting of results

Incremental costs and QALYs were reported, generating incremental cost-effectiveness ratios by metastatic and non-metastatic subgroups with a range of abiraterone discounts in deterministic sensitivity analysis. The study noted the primary reason for increased costs in the intervention arm was the cost of abiraterone, with the main reason for increased QALYs in the non-metastatic subgroup being the result of a longer duration in the hormone naive health states. There was a comprehensive set of key parameters varied in the probability sensitivity analysis, with base-case ICER results appearing robust to this variation. The study framed conclusions in the context of conventional cost-effectiveness thresholds to establish feasibility of implementation, highlighting that at list prices for the abiraterone it would be difficult to meet conditions of value for money to the NHS.

Study limitations

Although the economic study had access to outcome data from the STAMPEDE platform, this was an immature data cut[11]. Since 2017 further outcome data have become available in a STAMPEDE

meta-analysis, but this was not included in the economic model[10]. A median follow up of 40 months in the 2017 data cut imposed limitations on the economic model. Firstly, some health state transitions in the model had small event numbers which required joint survival models for groups of transitions, rather than preferred individual survival models. Furthermore, alternate parametric survival models, a key driver of most oncology economic models, were not included as part of sensitivity analysis. Secondly, the limited outcome data beyond onset of CRPC that were available for non-metastatic patients in transitions between select CRPC model health states required survival estimations in non-metastatic patients to be applied from metastatic patients who progressed to castration resistant disease. Finally, short term survival data (around 3 years) was used to extrapolate to a 45 year time horizon, creating potential uncertainty in these long term predictions. Utilising more recent outcome data may have aided in overcoming these issues and potentially increased confidence in results. It remains unknown what impact the use of updated outcome data would be if used in the model.

Costs included within the study were comprehensive, however the numerous regressions used for different costs categories added potential complexity to their application and interpretation. Although cost sources were clearly stated, the actual prices used for some medicines were unclear. However, chemotherapeutic agents' unit costs, abiraterone daily costs (£97.68/day), and mean daily cost for subsequent treatments (docetaxel, cabazitaxel, enzalutamide and radium-223) were stated. Missing doses for treatments within the trial also required imputation for the economic model, with values taken from the BNF. EQ-5D data were not routinely collected post-progression, which may have led to inaccurate health state utility values in post-progression health states. Comparative framing of utility values in the study was not presented.

Generalisability of results in NHS Scotland

There is high relevance of the patient population and selected subgroups, intervention, and comparator treatments to the proposal. As the STAMPEDE platform recruited from 111 UK and 5 Swiss sites, there can be confidence that survival and health related quality of life data collected reflects a UK patient population. Where the application of the results may be limited to NHS Scotland is the subsequent treatment proportions and costs. Firstly, the confidential PAS discounts of enzalutamide, cabazitaxel and radium-223 were not accounted for in the model through sensitivity analysis. Secondly, there was limited reporting of subsequent treatments in James et al 2017[11]. This presents uncertainty in the accuracy of proportionate use and estimated cost of subsequent treatments in the lifetime model. Thirdly, resource use within the economic model was estimated from clinician input or wider literature. As a result of these three limitations, total and incremental costs and QALYs may be subject to uncertainty and not fully reflective of practice in NHS Scotland. Although the base case ICERs were robust to utility and general disease management cost variation in probabilistic sensitivity analysis, subsequent treatment medicine costs were not part of this.

3.2 Council review | Cost-effectiveness evaluation

After considering all the available evidence, the Council were not satisfied that the case for cost effectiveness had been made.

As a consequence the Council was unable to support routine use of off-label abiraterone in this population at the present time.

4.0 Evidence Review Summary | Service Impact

The proposal estimates 450 eligible patients per year with an uptake of 50% in year 1 and thereafter reaching a steady state of 70-80% eligible patients. Patients will require monthly clinic visits initially with fortnightly liver enzyme tests for the first three months. Once patients are established and tolerating treatment, they may be transitioned to eight weekly or 12 weekly dispensing of abiraterone. The increased number of patients receiving treatment will have an impact on outpatient clinics with increased demand on medical, non-medical prescribing, clinical nurse specialists and dispensing services. Some NHS boards deliver abiraterone to patients through community pharmacy dispensing with oncology clinic review and prescribing of treatment, which requires a considerable amount of liaison and administration usually by the pharmacy team. Some patients may experience increased blood pressure while on treatment with abiraterone, management of which could pose additional burden on services.

5.0 Evidence Review Summary | Budget Impact

The change in treatment would increase the budget impact of treatment for this patient group. The list price of abiraterone (Zytiga) 500mg (56 tablets) is £2735, with a daily dose of 1000mg, and assumed 2 years of treatment. The cost per course in year 1 is expected to be £37,700, with a net drug budget impact of approximately £7.5 million (based on an estimated uptake of 200). The cost per course in year 2 is expected to be £73,300, with a net drug budget impact of approximately £25 million (based on an estimated uptake of 340). This is expected to be the steady state net drug budget impact. These estimates are based on list price and do not account for any commercial in confidence discounts.

6.0 Other Considerations

The abiraterone patent will expire later in 2022 and more competitively priced generic alternatives may be available thereafter. NCMAG will prioritise a rapid review of this proposal with updated health economic evaluation once generic alternatives are available.

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This advice represents the view of the National Cancer Medicines Advisory Group Council and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.